PALM INTRANET

Day : Friday
Date: 8/30/2002
Time: 13:35:06

Inventor Name Search Result

Your Search was:

Last Name = TIMMERS
First Name = C

Application#	Patent#	Status	Date Filed	Title	Inventor Name
60245756	Not Issued	020	11/03/2000	METHODS AND COMPOSITIONS FOR THE DIAGNOSIS AND TREATMENT OF CANCERS ASSOCIATED WITH DEFECTIVE DNA REPAIR MECHANISM	TIMMERS, C
09830227	Not Issued	030	06/11/2001	SERINE PROTEASE INHIBITOR	TIMMERS, C.M. CORNELIS MARIUS
09998027	Not Issued	020	11/02/2001	METHODS AND COMPOSITIONS FOR THE DIAGNOSIS OF CANCER SUSCEPTIBILITIES AND DEFECTIVE DNA REPAIR MECHANISMS AND TREATMENT THEREOF	TIMMERS, CYNTHIA
10165099	Not Issued	019	06/06/2002	METHODS AND COMPOSITIONS FOR THE DIAGNOSIS OF CANCER SUSCEPTIBILITIES AND DEFECTIVE DNA REPAIR MECHANISMS AND TREATMENT THEREOF	TIMMERS, CYNTHIA

Inventor Search Completed: No Records to Display.

Search Another: Inventor

Last Name timmers **First Name** c

Search

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Back to PALM | ASSIGNMENT | OASIS | Home page

[redacted]

09/ 876,964

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 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
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 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 09  JAPIO to be reloaded August 25, 2002
 NEWS 20  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 21  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 22  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 23  Aug 26  Sequence searching in REGISTRY enhanced

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'HOME' ENTERED AT 16:43:50 ON 30 AUG 2002

09/ 876,964

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=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:43:58 ON 30 AUG 2002
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STRUCTURE FILE UPDATES:   29 AUG 2002  HIGHEST RN 445455-71-0
DICTIONARY FILE UPDATES:  29 AUG 2002  HIGHEST RN 445455-71-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09830227.str

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 16:44:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   1268 TO ITERATE

 78.9% PROCESSED    1000 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        23225 TO    27495
PROJECTED ANSWERS:            1554 TO     2806

L2           50 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 16:44:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  25325 TO ITERATE

100.0% PROCESSED   25325 ITERATIONS                        2396 ANSWERS
SEARCH TIME: 00.00.02

L3         2396 SEA SSS FUL L1

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       1479811 BENZO
       1325025 WITH
        220862 TRIAZIN?
             0 BENZO WITH TRIAZIN?
               (BENZO(W)WITH(W)TRIAZIN?)
L4        2396 L3 NOT (BENZO WITH TRIAZIN?)

=> file caplus
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[redacted]

09/ 876,964

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	153.04	153.25

FILE 'CAPLUS' ENTERED AT 16:46:00 ON 30 AUG 2002
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FILE COVERS 1907 - 30 Aug 2002 VOL 137 ISS 10
FILE LAST UPDATED: 29 Aug 2002 (20020829/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l4
L5         3101 L4

=> s l5 and (amino adj acid)
         842669 AMINO
            198 ADJ
        3365872 ACID
              0 AMINO ADJ ACID
                  (AMINO(W)ADJ(W)ACID)
L6            0 L5 AND (AMINO ADJ ACID)

=> s l5 and (amino acid)
         842669 AMINO
        3365872 ACID
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u
SEARCH ENDED BY USER

=> s l5 and (amino acid)
         842669 AMINO
<------User Break------>
u
SEARCH ENDED BY USER

=> s (amino acid)
         842669 AMINO
        3365872 ACID
L7       427027 (AMINO ACID)
                (AMINO(W)ACID)

=> s l5 and l7
L8           39 L5 AND L7
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[redacted]

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=> d l8 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 39 ANSWERS - CONTINUE? Y/(N):y

L8   ANSWER 1 OF 39  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:556104  CAPLUS
DOCUMENT NUMBER:         137:109489
TITLE:                   Compositions comprising a polypeptide and an active
                         agent
INVENTOR(S):             Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal
                         J.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 34 pp., which which which which
                         which which which which which which which which which
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     US 2002099013      A1   20020725       US 2001-933708   20010822
PRIORITY APPLN. INFO.:                   US 2000-247556P  P  20001114
                                         US 2000-247558P  P  20001114
                                         US 2000-247559P  P  20001114
                                         US 2000-247560P  P  20001114
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                                         US 2000-247611P  P  20001114
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                                         US 2000-247621P  P  20001114
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                                         US 2000-247927P  P  20001114
                                         US 2000-247928P  P  20001114
                                         US 2000-247929P  P  20001114
                                         US 2000-247930P  P  20001114
```
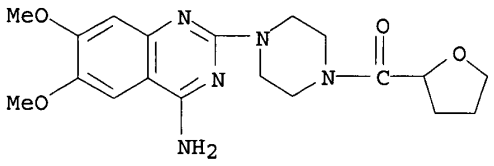

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the compn. to the patient. The peptide is a homopolymer of a naturally occurring **amino acid** or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepd. from Glu(OBut)NCA and cephalexin hydrochloride.

IT **63074-08-8**, Terazosin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

RN 63074-08-8 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L8 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:332011 CAPLUS

DOCUMENT NUMBER: 136:355482

TITLE: Compositions comprising a polypeptide and an active agent

INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J.

PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034237	A1	20020502	WO 2001-US26142	20010822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-642820 A 20000822

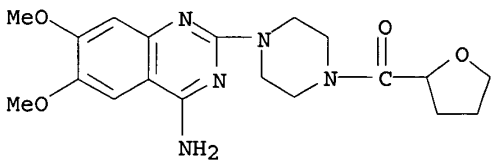
AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the compn. to the patient. The peptide is a homopolymer of a naturally occurring **amino acid** or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepd. from Glu(OBut)NCA and

cephalexin hydrochloride.

IT **63074-08-8**, Terazosin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

RN 63074-08-8 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:246274 CAPLUS

DOCUMENT NUMBER: 136:397222

TITLE: The NMDA receptor ion channel: a site for binding of huperzine A

AUTHOR(S): Gordon, Richard K.; Nigam, Savita V.; Weitz, Julie A.; Dave, Jitendra R.; Doctor, Bhupendra P.; Ved, Haresh S.

CORPORATE SOURCE: Division of Biochemistry, Walter Reed Army Institute of Research, Washington, DC, 20307-5100, USA

SOURCE: Journal of Applied Toxicology (2001), 21(Suppl. 1), S47-S51
CODEN: JJATDK; ISSN: 0260-437X

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

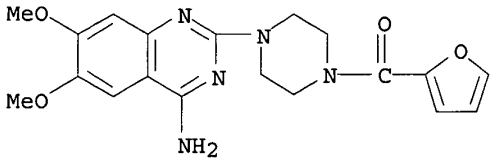
AB Huperzine A (HUP-A), first isolated from the Chinese club moss Huperzia serrata, is a potent, reversible and selective inhibitor of acetylcholinesterase (AChE) over butyrylcholinesterase (BChE) (Life Sci. 54: 991-997). Because HUP-A has been shown to penetrate the blood-brain barrier, is more stable than the carbamates used as pretreatments for organophosphate poisoning (OP) and the HUP-A:AChE complex has a longer half-life than other prophylactic sequestering agents, HUP-A has been proposed as a pretreatment drug for nerve agent toxicity by protecting AChE from irreversible OP-induced phosphonylation. More recently (NeuroReport 8: 963-968), pretreatment of embryonic neuronal cultures with HUP-A reduced glutamate-induced cell death and also decreased glutamate-induced calcium mobilization. These results suggest that HUP-A might interfere with and be beneficial for excitatory **amino acid** overstimulation, such as seen in ischemia, where persistent elevation of internal calcium levels by activation of the N-methyl-D-aspartate (NMDA) glutamate subtype receptor is found. The authors have now investigated the interaction of HUP-A with glutamate receptors. Freshly frozen cortex or synaptic plasma membranes were used, providing 60-90% specific radioligand binding. Huperzine A (.ltoreq.100 .mu.M) had no effect on the binding of [3H]glutamate (low- and high-affinity glutamate sites), [3H]MDL 105,519 (NMDA glycine regulatory site), [3H]ifenprodil (NMDA polyamine site) or [3H]CGS 19755 (NMDA

antagonist). In contrast with these results, HUP-A non-competitively (Hill slope < 1) inhibited [3H]MK-801 and [3H]TCP binding (co-located NMDA ion channel PCP site) with pseudo Ki .apprx. 6 .mu.M. Furthermore, when neuronal cultures were pretreated with HUP-A for 45 min prior to NMDA exposure, HUP-A dose-dependently inhibited the NMDA-induced toxicity. Although HUP-A has been implicated to interact with cholinergic receptors, it was without effect at 100 .mu.M on muscarinic (measured by inhibition of [3H]QNB or [3H]NMS binding) or nicotinic [3H]epibatidine binding) receptors; also, HUP-A did not perturb adenosine receptor binding [3H]PIA or [3H]NECA). Therefore, HUP-A most likely attenuates excitatory **amino acid** toxicity by blocking the NMDA ion channel and subsequent Ca2+ mobilization at or near the PCP and MK-801 ligand sites. Thus, on the one hand, HUP-A could be used as a pretreatment against OPs and it might also be a valuable therapeutic intervention in a variety of acute and chronic disorders by protecting against overstimulation of the excitatory **amino acid** pathway. By blocking NMDA ion channels without psychotomimetic side-effects, HUP-A may protect against diverse neurodegenerative states obsd. during ischemia or Alzheimer's disease.

IT **19216-56-9**, Prazosin
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NMDA receptor ion channel a site for binding of huperzine A)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:781185 CAPLUS

DOCUMENT NUMBER: 135:328176

TITLE: Polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses

INVENTOR(S): Liggett, Stephen B.; Small, Kirsten M.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079561	A2	20011025	WO 2001-US12575	20010417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

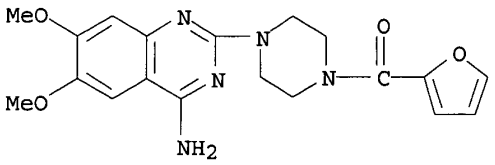
PRIORITY APPLN. INFO.: US 2000-551744 A 20000417
US 2000-636259 A 20000810
US 2000-692077 A 20001019

AB The present invention includes polymorphisms in nucleic acids encoding the .alpha.2B, .alpha.2A, and .alpha.2C adrenergic receptor genes and expressed .alpha.2B, .alpha.2A and .alpha.2C adrenergic receptor protein mol. The invention also pertains to methods and mols. for detecting such polymorphisms. The invention further pertains to the use of such mols. and methods in the diagnosis and treatment of diseases such as cardiovascular and central nervous system disease. Genetic polymorphisms of deletion/insertions and single nucleotides in the intracellular loop 3 region of human .alpha.2 adrenergic receptors were identified and characterized to search for correlations between the polymorphisms and physiol. signaling functions of the receptors. Recombinant polymorphic receptor proteins were expressed in cell lines to measure ligand binding, protein phosphorylation, effect on adenyl cyclase activity, MAP kinase activation, GTP.gamma.S binding, and/or inositol phosphate accumulation. Differences in signal transduction due to the .alpha.2 adrenoceptor polymorphisms were obsd. but the polymorphisms have not yet been genetically linked with disease, for example hypertension. The polymorphisms of this invention can be used to det. an individual's risk for developing a disease, for diagnosis, and for selecting appropriate drug treatments based on the identity of the polymorphism.

IT **19216-56-9**, Prazosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:626800 CAPLUS

DOCUMENT NUMBER: 135:366874

TITLE: Molecular cloning and functional expression of the guinea pig .alpha.1a-adrenoceptor

AUTHOR(S): Gonzalez-Espinosa, C.; Romero-Avila, M. T.; Mora-Rodriguez, D. M.; Gonzalez-Espinosa, D.; Garcia-Sainz, J. A.

CORPORATE SOURCE: Departamento de Biologia Celular, Universidad Nacional Autonoma de Mexico, Instituto de Fisiologia Celular, Mexico City, 04510, Mex.

SOURCE: European Journal of Pharmacology (2001), 426(3), 147-155
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

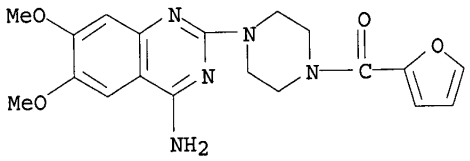
AB In the present paper, the cloning and expression of the guinea pig .alpha.1A-adrenoceptor is presented. The nucleotide sequence had an open reading frame of 1401 bp that encoded a 466 **amino-acid**

[redacted]

protein with an estd. mol. mass of .apprxeq.51.5 kDa. When the clone was expressed in Cos-1 cells, specific high-affinity binding of [3H]prazosin and [3H]tamsulosin was obsd. Chloroethylclonidine treatment of membranes slightly decreased the total binding with both radioligands. Binding competition expts. using [3H]tamsulosin showed the following potency order: (a) for agonists: oxymetazoline.mchgt.epinephrine>norepinephrine>me thoxamine, and (b) for antagonists: prazosin.gtoreq.5-methyl-urapidil=benoxathian>phentolamine.mchgt.BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7,9-dione). Photoaffinity labeling using [125I-aryl]azido-prazosin revealed a major broad band with a mol. mass between 70 and 80 kDa. The receptor was functional, as evidenced by an epinephrine-increased prodn. of [3H]inositol phosphates that was blocked by prazosin.

IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mol. cloning, functional expression and pharmacol. characterization of guinea pig .alpha.1a-adrenoceptor)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:348246 CAPLUS
DOCUMENT NUMBER: 135:103985
TITLE: Identification and localization of three photobinding sites of iodoarylazidoprazosin in hamster P-glycoprotein
AUTHOR(S): Isenberg, Barbel; Thole, Hubert; Tummler, Burkhard; Demmer, Annette
CORPORATE SOURCE: Klinische Forschergruppe, Zentrum Biochemie and Zentrum Kinderheilkunde, Medizinische Hochschule Hannover, Hannover, D-30625, Germany
SOURCE: European Journal of Biochemistry (2001), 268(9), 2629-2634
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

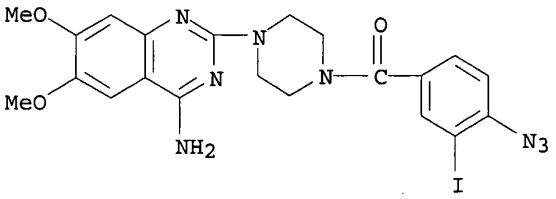
AB P-glycoprotein is an ATP-dependent drug-efflux pump which can transport a diverse range of structurally and functionally unrelated substrates across the plasma membrane. Overexpression of this protein may result in multidrug resistance and is a major cause of the failure of cancer chemotherapy. The most commonly used photoreactive substrate is iodoarylazidoprazosin. Its binding domains within the P-glycoprotein have so far been inferred from indirect methods such as epitope mapping. In this study, the binding sites were refined and relocalized by direct anal. of photolabeled peptides. P-glycoprotein-contg. plasma membrane vesicles of Chinese hamster ovary B30 cells were photoaffinity-labeled with iodoarylazidoprazosin. After chem. cleavage behind tryptophan residues or

enzymic cleavage behind lysine residues, the resulting 125I-labeled peptides were sepd. by tricine/PAGE and HPLC and subjected to Edman sequencing. The major photoaffinity binding sites of iodoarylazidoprazosin were localized in the **amino-acid** regions 248-312 [transmembrane segment (TM)4 to TM5], 758-800 (beyond TM7 to beyond TM8) and 1160-1218 (after the Walker A motif of the second nucleotide-binding domain). Therefore the binding pocket of iodoarylazidoprazosin is made up of at least three binding epitopes.

IT **90990-97-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(identification and localization of three photobinding sites of iodoarylazidoprazosin in hamster P-glycoprotein)

RN 90990-97-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(4-azido-3-iodobenzoyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:279642 CAPLUS

DOCUMENT NUMBER: 134:249866

TITLE: The role of central catecholaminergic systems in regulation of food intake of chicks

AUTHOR(S): Bungo, Takashi; Ando, Ryuichi; Kawakami, Sinichi; Ohgushi, Atsushi; Furuse, Mitsuhiro

CORPORATE SOURCE: Lab. Animal Sci., Dep. Agribiol. Sci., Fac. Agric., Ehime Univ., Matsuyama, 790-8566, Japan

SOURCE: Journal of Poultry Science (2001), 38(1), 35-40
CODEN: JPSOBX

PUBLISHER: Japan Poultry Science Association

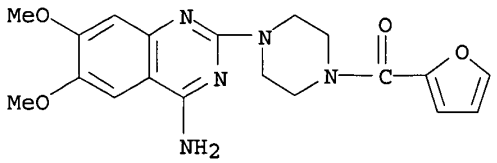
DOCUMENT TYPE: Journal

LANGUAGE: English

AB To clarify catecholaminergic systems on the regulation of food intake in the neonatal chick, we examd. the effects of intracerebroventricular (ICV) injection of prazosin (.alpha.1-adrenoceptor antagonist), yohimbine (.alpha.2-adrenoceptor antagonist), and benserazide (an inhibitor of L-arom. **amino acid** decarboxylase). We found that food intake was significantly suppressed by ICV injection of yohimbine (25 and 50 .mu.g) over 60 min ($P < 0.05$). Any doses of prazosin (1.25, 2.5 and 5.0 .mu.g) did not alter food intake of chicks ($P > 0.05$). ICV administration of benserazide induced a hypophagia after 60 min postinjection ($P < 0.05$). It is suggested that catecholaminergic systems play an important role in the neural regulation of food intake in chicks, esp. through .alpha.2-adrenoceptor.

IT **19216-56-9**, Prazosin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(role of central catecholaminergic system in regulation of food intake of chicks)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)-
(9CI) (CA INDEX NAME)

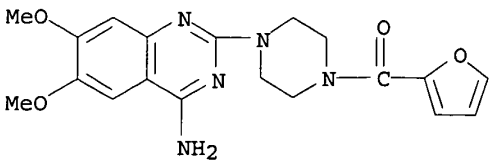


L8 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:152504 CAPLUS
DOCUMENT NUMBER: 134:202707
TITLE: Modulation of the blood-brain barrier transporter for leptin
INVENTOR(S): Banks, William A.
PATENT ASSIGNEE(S): Tulane University, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013935	A2	20010301	WO 2000-US23110	20000823

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-150300P P 19990823
AB Nervous system agents and methods for modulating the transport of leptin across the blood-brain barrier are disclosed.
IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(modulation of the blood-brain barrier transporter for leptin)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)-
(9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:454237 CAPLUS
DOCUMENT NUMBER: 133:84227
TITLE: Sequences of human .alpha.-1a, .alpha.-1b, and .alpha.-1c adrenergic receptors, synthesis and activity of antagonist thereof, and drug screening assays
INVENTOR(S): Bard, Jonathon A.; Weinshank, Richard L.; Forray, Carlos
PATENT ASSIGNEE(S): Synaptic Pharmaceuticals Corporation, USA
SOURCE: U.S., 83 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

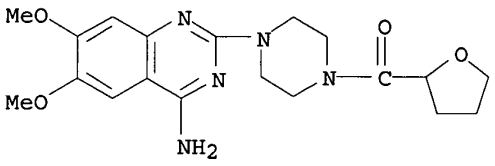
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6083705	A	20000704	US 1998-206899	19981207
US 6156518	A	20001205	US 1999-474551	19991229

PRIORITY APPLN. INFO.: US 1998-206899 A1 19981207

AB The invention provides protein and DNA sequences of human .alpha.-1a, .alpha.-1b, and .alpha.-1c adrenergic receptors. This invention also relates to drug screening assays and pharmaceutical compds. related to the disclosed .alpha.-1 adrenergic receptors. The invention also discloses the synthesis and binding potency of .alpha.-1 antagonists and their ability to inhibit prostate smooth muscle contraction. This invention provides nucleic acid probes, and antisense oligonucleotides complementary to .alpha.-1a, .alpha.-1b and .alpha.-1c adrenergic receptor genes. This invention further relates to treatments for alleviating abnormalities assocd. with the disclosed .alpha.-1 adrenergic receptors.

IT **63074-08-8P**, Terazosin hydrochloride
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antagonist; sequences of human .alpha.-1a, .alpha.-1b, and .alpha.-1c adrenergic receptors, synthesis and activity of antagonist thereof, and drug screening assays)

RN 63074-08-8 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

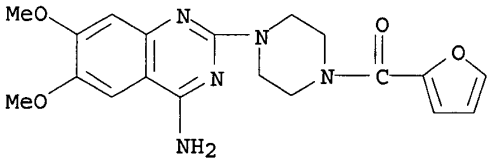
L8 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:345446 CAPLUS
DOCUMENT NUMBER: 133:99703

[redacted]

TITLE: Cloning of rabbit .alpha.1b-adrenoceptor and pharmacological comparison of .alpha.1a-, .alpha.1b- and .alpha.1d-adrenoceptors in rabbit
AUTHOR(S): Piao, H.; Taniguchi, T.; Nakamura, S.; Zhu, J.; Suzuki, F.; Mikami, D.; Muramatsu, I.
CORPORATE SOURCE: School of Medicine, Department of Pharmacology, Fukui Medical University, Matsuoka, Fukui, 910-1193, Japan
SOURCE: European Journal of Pharmacology (2000), 396(1), 9-17
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have isolated a cDNA clone of the rabbit .alpha.1b-adrenoceptor which has an open reading frame of 1557 nucleotides encoding a protein of 518 amino acids. The sequence shows higher identity to those of hamster, human, and rat .alpha.1b-adrenoceptors than to those of rabbit .alpha.1a- and .alpha.1d-adrenoceptors. The pharmacol. binding properties of this clone expressed in Cos-7 cells showed a characteristic profile as .alpha.1b-adrenoceptor; high affinity for prazosin (pKi=10.3), relatively high affinity for tamsulosin (9.5) and low affinity for KMD 3213 (8.5), WB 4101 (8.7), and BMY 7378 (7.3). We have compared the levels of mRNA expression of three .alpha.1-adrenoceptor subtypes in rabbit tissues using the competitive reverse transcription/polymerase chain reaction (RT/PCR) assay. In most rabbit tissues except heart, .alpha.1a-adrenoceptor mRNA was expressed 10 folds more than the other two subtypes. However, binding expts. with [3H]prazosin and [3H]KMD 3213 in rabbit tissues revealed a poor relationship between binding d. and mRNA level. Esp., .alpha.1b binding sites were exclusively predominant in spleen, whereas the .alpha.1b subtype was minor at the mRNA level. These results indicate a high identity of structural and pharmacol. profiles of three distinct .alpha.1-adrenoceptor subtypes between rabbit and other species, but there are species differences in their distribution.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rabbit .alpha.1b-adrenoceptor sequence and expression and pharmacol. comparison with other .alpha.1-adrenoceptor subtypes)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

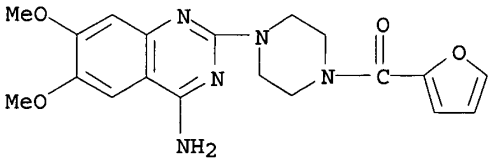
L8 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:309881 CAPLUS
DOCUMENT NUMBER: 133:69131
TITLE: Splice isoforms of .alpha.1a-adrenoceptor in rabbit
AUTHOR(S): Suzuki, Fumiko; Taniguchi, Takanobu; Takauji, Rumiko; Murata, Satoshi; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: British Journal of Pharmacology (2000), 129(8), 1569-1576

CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two splice isoforms of rabbit .alpha.1a-adrenergic receptor (AR), (named .alpha.1a-OCU.2-AR and .alpha.1a-OCU.3-AR) have been isolated from the liver cDNA library in addn. to the previously reported isoform (.alpha.1a-OCU.1-AR). Although they have the identical splice position with human .alpha.1a-AR isoforms, the C-terminal sequences are distinct from those of human isoforms. Among these rabbit .alpha.1a-AR isoforms, there are no significant differences in pharmacol. properties: high affinity for prazosin, WB 4101, KMD-3213 and YM 617 and low affinity for BMY 7378, using COS-7 cells expressing each isoform by radioligand binding assay. Competitive reverse transcription-polymerase chain reaction (RT-PCR) anal. revealed that mRNA of .alpha.1a-ARs was expressed in liver, thoracic aorta, brain stem and thalamus of rabbit. The splice isoforms exhibited a distinct distribution pattern in rabbit; .alpha.1a-OCU.1-AR was expressed most abundantly in those tissues. CHO clones, stably expressing each isoforms with receptor d. 740 fmol mg-1 protein in .alpha.1a-OCU.1-AR, 1200 fmol mg-1 in .alpha.1a-OCU.2-AR and 570 fmol mg-1 in .alpha.1a-OCU.3-AR, resp., showed a noradrenaline-induced increase in inositol trisphosphate which was suppressed by prazosin. Noradrenaline elicited a concn.-dependent increase in extracellular acidification rate (EAR) in the CHO clones with pEC50 values of 6.19 for .alpha.1a-OCU.1-AR, 6.49 for .alpha.1a-OCU.2-AR and 6.58 for .alpha.1a-OCU.3-AR, resp. Noradrenaline caused a concn.-dependent increase in intracellular Ca2+ concn. ([Ca2+]i) in the CHO clones with pEC50 values of 6.14 for .alpha.1a-OCU.1-AR, 7.25 for .alpha.1a-OCU.2-AR and 7.70 for .alpha.1a-OCU.3-AR, resp. In conclusion, the present study shows the occurrence of three splice isoforms of rabbit .alpha.1a-AR, which are unique in C-terminal sequence and in tissue distribution. They show similar pharmacol. profiles in binding studies but .alpha.1a-OCU.3-AR had the highest potency of noradrenaline in functional studies in spite of the lowest receptor d. These findings suggest that the structure of C-terminus of .alpha.1a-ARs may give the characteristic functional profile.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.1a-adrenoceptor splice isoform sequence and functional expression and pharmacol. characterization in rabbit)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:291003 CAPLUS
DOCUMENT NUMBER: 132:322143
TITLE: Preparation of isoquinoline **amino acid** derivatives as serine protease inhibitors.

[redacted]

09/ 876,964

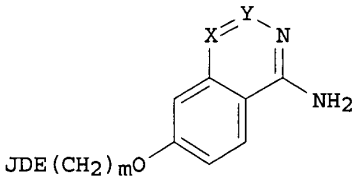
INVENTOR(S): Timmers, Cornelis Marius; Rewinkel, Johannes Bernardus Maria
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Applicant(s)

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024718	A1	20000504	WO 1999-EP7928	19991019
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963413	A1	20000515	AU 1999-63413	19991019
BR 9914694	A	20010710	BR 1999-14694	19991019
EP 1123280	A1	20010816	EP 1999-950761	19991019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001001966	A	20010423	NO 2001-1966	20010420

PRIORITY APPLN. INFO.: EP 1998-203559 A 19981023
WO 1999-EP7928 W 19991019

OTHER SOURCE(S): MARPAT 132:322143
GI



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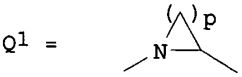


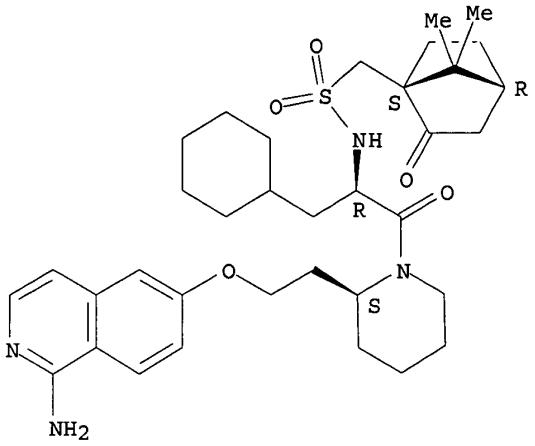
AB Title compds. [I; J = H, R1, R1O2C, R1CO, R1SO2, etc.; D = NHCHR1CO, D-1-Tiq, D-Atc, Aic, D-1-Piq, etc.; E = NR2CH2, (substituted) Q1; R1 = (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkylene; R2 = H, R1; X, Y = CH, N, both may not = N; m = 1, 2; p = 2-4], were prepd. Thus, (2S)-1-[N-(-)-camphorsulfonyl-D-cyclohexylalaninyl]-2-[2-(1-aminoisoquinolin-6-oxy)ethyl]piperidine (soln. phase prepn. given) showed antithrombin activity with IC50 = 0.41.mu.M.

IT **266690-33-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of isoquinoline **amino acid** derivs. as serine protease inhibitors)

RN 266690-33-9 CAPLUS

CN Piperidine, 2-[2-[(1-amino-6-isoquinolinyl)oxy]ethyl]-1-[(2R)-3-cyclohexyl-2-[[[[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]amino]-1-oxopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:102899 CAPLUS
DOCUMENT NUMBER: 132:218198
TITLE: Investigation of the hemodynamic effects of Phoneutria nigriventer venom in anesthetized rabbits
AUTHOR(S): Estato, Vanessa; Antunes, Edson; Machado, Bianca; De Nucci, Gilberto; Tibirica, Eduardo
CORPORATE SOURCE: Departamento de Fisiologia e Farmacodinamica, Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, 21045-900, Brazil
SOURCE: Toxicon (2000), 38(6), 841-853
CODEN: TOXIA6; ISSN: 0041-0101
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

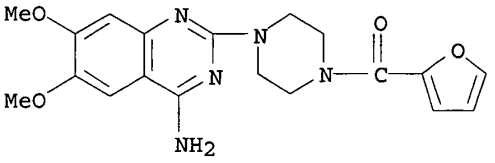
AB The hemodynamic alterations induced by the central and peripheral administration of the armed spider (P. nigriventer) venom (PNV) were investigated in anesthetized rabbits. The intracerebroventricular injection of increasing doses of PNV (30 and 100 .mu.g/kg) elicited a biphasic cardiovascular response characterized by a brief hypotension (1-3 min) followed by a marked and sustained (>30 min) increase in mean arterial pressure (61 .+-. 5 and 61 .+-. 10%, resp.) and in systemic vascular resistance (135 .+-. 21 and 161 .+-. 37%) accompanied by mild increases in cardiac contractility. Systemic alterations such as salivation and muscular fasciculation were also obsd. At the opposite, the dose of 100 .mu.g/kg PNV injected i.v. produced only a hypotensive effect (29 .+-. 4% decrease in mean arterial pressure) and a decrease in vascular resistance (38 .+-. 5%). Nevertheless, a much higher dose of PNV (1 mg/kg) injected i.v. produced a hypertensive response analogous to the one obsd. upon central administration. The central hypertensive response induced by PNV was not affected by preteating the animals with selective antagonists of receptors of different neurotransmitters or endogenous mediators such as: acethylcoline muscarinic, bradykinin B2, angiotensin II AT1 receptors, and also antagonists of the excitatory **amino acid** receptors of the central nervous system. Nevertheless, the i.v. pretreatment with the selective .alpha.1-adrenergic receptor antagonist prazosin significantly blunted the excitatory cardiovascular response evoked by the central injection of PNV. Thus, PNV can induce central as well as peripheral hemodynamic effects. The central component seems to be mediated by the activation of cardiovascular centers which in

turn lead to an increase in the sympathetic outflow to the periphery whereas the peripheral component can be accounted for either by direct activation of the vascular .alpha.1-adrenergic receptors or by catecholamine release from the sympathetic nerve endings.

IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prazosin effect on hemodynamic effects of Phoneutria nigriventer venom)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:796049 CAPLUS
DOCUMENT NUMBER: 132:30810
TITLE: Method of identifying antidepressant compounds using cells expressing an .alpha.1b-adrenergic receptor and transport-P protein
INVENTOR(S): Al-Damluji, Saad
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964861	A2	19991216	WO 1999-GB1859	19990611
WO 9964861	A3	20000629		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9942829	A1	19991230	AU 1999-42829	19990611

PRIORITY APPLN. INFO.: GB 1998-12624 A 19980611
WO 1999-GB1859 W 19990611

OTHER SOURCE(S): MARPAT 132:30810

AB A method for identifying compds. having antidepressant activity comprises: (a) contacting a cell expressing an .alpha.1b-adrenergic receptor and transport-P protein with the compd. to be tested; (b) prior to or after step (a), contacting the compd. with a cell expressing an .alpha.1b-adrenergic receptor but not transport-P protein; and (c) selecting a compd. which preferentially binds transport P. Compds.

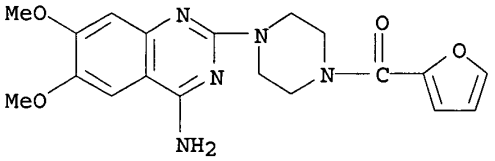
[redacted]

identified using the method of the invention are also provided, as well as pharmaceutical compns. contg. them and their use in treating depression.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antidepressant identification with cells expressing .alpha.1b-adrenergic receptor and transport-P protein)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:53380 CAPLUS

DOCUMENT NUMBER: 130:120479

TITLE: Nucleic acids encoding human alpha 1 adrenergic receptors, vectors containing the nucleic acid, and cells containing the vectors

INVENTOR(S): Bard, Jonathan A.; Weinshank, Richard L.; Forray, Carlos

PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corporation, USA

SOURCE: U.S., 80 pp., Cont.-in-part of U.S. Ser. No. 952,798, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861309	A	19990119	US 1995-406855	19950821
WO 9408040	A1	19940414	WO 1993-US9187	19930924
W: AU, BR, CA, FI, HU, JP, KR, NO, NZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1063291	A2	20001227	EP 2000-119362	19930924
EP 1063291	A3	20010425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1063292	A2	20001227	EP 2000-119363	19930924
EP 1063292	A3	20010425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5556753	A	19960917	US 1994-334698	19941104
US 5714381	A	19980203	US 1995-468939	19950606
AU 9734207	A1	19980129	AU 1997-34207	19970815
AU 718197	B2	20000406		

PRIORITY APPLN. INFO.:
US 1992-952798 B2 19920925
WO 1993-US9187 W 19930924
US 1992-952789 A2 19920925
EP 1993-922758 A3 19930924
US 1994-334698 A1 19941104

AB The nucleic acids encoding human .alpha.1a- and .alpha.1b-adrenergic receptors, vectors contg. these nucleic acids, and transformed cells transformed with these vectors are disclosed. The cDNAs for human .alpha.1a-, .alpha.1b- and .alpha.1c-adrenergic receptors were cloned.

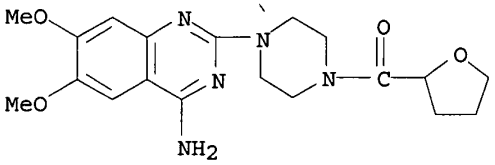
[redacted]

The cDNAs were expressed in LM(tk-) cells using pCEXV-3 and the identities of the receptors were confirmed by their pharmacologies. A series of potential antagonists (Terazosin, Indoramin, benzamidopiperidines, SKF-104856) were prepd. and tested for their efficacy in treatment of benign prostatic hyperplasia. Those antagonists most selective for the .alpha.1c-adrenergic receptor were found to be most effective.

IT **63074-08-8P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(nucleic acids encoding human alpha 1 adrenergic receptors, vectors contg. nucleic acid, and cells contg. vectors)

RN 63074-08-8 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetrahydro-2-furanyl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:330439 CAPLUS
DOCUMENT NUMBER: 129:90765
TITLE: Molecular cloning, expression and characterization of cDNA encoding a mouse .alpha.1a-adrenoceptor
AUTHOR(S): Xiao, Lei; Scofield, Margaret A.; Jeffries, William B.
CORPORATE SOURCE: Department of Pharmacology, Creighton University School of Medicine, Omaha, NE, 68178, USA
SOURCE: British Journal of Pharmacology (1998), 124(1), 213-221
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, we have cloned, expressed, and characterized an .alpha.1a-adrenoceptor gene from the mouse. We designed oligonucleotide PCR primers complementary to regions of the rat .alpha.1a-adrenoceptor sequence and amplified cDNA fragments from total RNA of mouse cerebral cortex, liver and kidney by reverse transcription-polymerase chain reaction (RT-PCR). Both the nucleotide and deduced peptide sequences of the cDNA showed high sequence identity with those of cloned .alpha.1a-adrenoceptors from other species. The cDNA clone had an open reading frame of 1398 nucleotides encoding a 466 **amino acid** peptide which had 97%, 92% and 90% identity with the deduced **amino acid** sequences of the rat, human and bovine .alpha.1a-adrenoceptor, resp. The amplified mouse cDNA was inserted into a mammalian expression vector pcDNA3.1(+) and expressed in COS-1 cells. The pharmacol. properties of the mouse cDNA clone were examd. in radioligand binding studies and functional assays. The expressed mouse

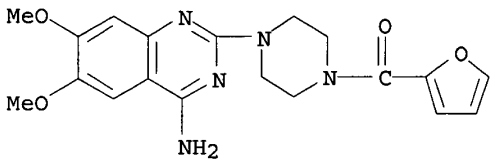
[redacted]

protein had a high affinity for [3H]-prazosin (Kd=0.48 nM) and pattern of affinity for antagonists in competition studies that is similar to that of the rat .alpha.1a-adrenoceptor. Chloroethylclonidine (CEC) could slowly alkylate the expressed protein, with a rate similar to that of the rat .alpha.1a-adrenoceptor. The expressed receptors were able to mediate noradrenaline (NA) stimulation of the prodn. of inositol phosphates in COS-1 cells, consistent with coupling to phospholipase C. This response to NA could be reversed by pretreatment of the transfected cells with prazosin. Based on the above evidence, we concluded that the cloned cDNA is that of the mouse .alpha.1a-adrenoceptor.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. properties of the mouse .alpha.1a-adrenoceptor expressed in COS-1 cells, high affinity for prazosin and pattern of affinity for antagonists in competition studies similar to that of rat .alpha.1a-adrenoceptor)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:578770 CAPLUS

DOCUMENT NUMBER: 127:274531

TITLE: Hydrolytic profile for ester- or amide-linkage by carboxylesterases pI 5.3 and 4.5 from human liver

AUTHOR(S): Takai, Satomi; Matsuda, Ayuka; Usami, Yoshiko; Adachi, Tetsuo; Sugiyama, Tadashi; Katagiri, Yoshihiro; Tatematsu, Masae; Hirano, Kazuyuki

CORPORATE SOURCE: Department of Pharmaceutics, Gifu Pharmaceutical University, Gifu, 502, Japan

SOURCE: Biological & Pharmaceutical Bulletin (1997), 20(8), 869-873
CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

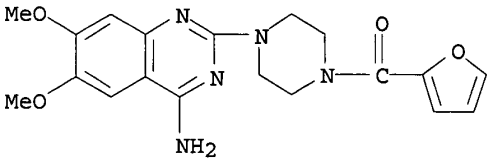
AB Carboxylesterases (EC 3.1.1.1) from human liver were purified using Q-Sepharose, Sephadex G-150, isoelectrofocusing and Con A-Sepharose. The calcd. mol. mass of the pI 5.3 enzyme was 120 kDa and 61 kDa from the results of Sephadex G-150 gel filtration and SDS-PAGE, resp., suggesting that this enzyme is a dimer. On the other hand, carboxylesterase pI 4.5, with a mol. mass of 64 kDa, was a monomer. The activities of both enzymes were inhibited by typical serine enzyme inhibitors. **Amino acid** sequence anal. of the purified enzymes pI 5.3 and 4.5 showed high homol. with rabbit carboxylesterase form 1 and 2, resp. The results also suggested that carboxylesterase pI 5.3 is identical to the deduced **amino acid** sequence from cDNA for HU1, and that carboxylesterase pI 4.5 is identical to the deduced **amino acid** sequence from the cDNA registered as human carboxylesterase (hCE-2) in GenBank. The authors first purified carboxylesterase pI 4.5 and investigated its hydrolytic activity upon various drugs. The two enzymes differed in substrate specificity. Prodrugs of

angiotensin-converting enzyme inhibitors, such as delapril and imidapril, were converted to active metabolites by carboxylesterase pI 5.3, but not by carboxylesterase pI 4.5. The hydrolysis velocity of temocapril by carboxylesterase pI 5.3 was 12-fold faster than by carboxylesterase pI 4.5. In contrast, aspirin, oxybutynin and procaine were hydrolyzed by only carboxylesterase pI 4.5. The authors also found that an amide-linkage in drugs, except for that in aniracetam, was not a good substrate for the two enzymes. Consequently, carboxylesterases pI 5.3 and 4.5 may be involved in the metab. of various drugs contg. an ester-linkage.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(purifn. and partial **amino acid** sequence of pI 5.3 and 4.5 carboxylesterases from human liver and kinetic parameters of hydrolysis of drugs contg. ester- or amide-linkages)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:304650 CAPLUS

DOCUMENT NUMBER: 127:76362

TITLE: Cloning, functional expression and tissue distribution of rabbit .alpha.1a-adrenoceptor

AUTHOR(S): Miyamoto, Sayako; Taniguchi, Takanobu; Suzuki, Fumiko; Takita, Manabu; Kosaka, Nobuyuki; Negoro, Eiju; Okuda, Tomoyuki; Kosaka, Hirotaka; Murata, Satoshi; Nakamura, Seigo; Akagi, Yoshio; Oshita, Masafumi; Watanabe, Yoshinari; Muramatsu, Ikunobu

CORPORATE SOURCE: Departments Pharmacology and Ophthalmology, Fukui Medical School, Matsuoka, 910-11, Japan

SOURCE: Life Sciences (1997), 60(23), 2069-2074
CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A cDNA clone, which has an open reading frame of 1398 nucleotides encoding a 466-**amino acid** peptide, has been isolated from rabbit liver cDNA library. Compared with the peptide sequence, it shows high homol. to .alpha.1a adrenoceptors of human, bovine and rat. The authors expressed this clone in COS-7 and investigated the pharmacol. properties, revealing similarity to those of human .alpha.1a adrenoceptors. Competitive RT/PCR has detected the mRNA in variety of rabbit tissues, esp. abundantly in liver, vas deferens, brain, and aorta, but not in heart.

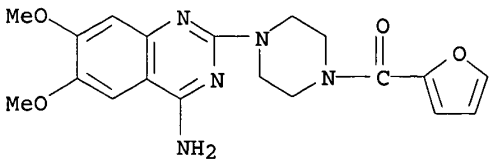
IT **19216-56-9**, Prazosin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cloning, functional expression and tissue distribution of rabbit .alpha.1a-adrenoceptor)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)-

[redacted]

(9CI) (CA INDEX NAME)



L8 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:254669 CAPLUS
DOCUMENT NUMBER: 124:280128
TITLE: mutant gene in transfected COS-1 cell produces constitutively activating adrenergic receptor with preference for the phospholipase C pathway and use of cell for screening epinephrine and other compds.
INVENTOR(S): Graham, Robert; Perez, Dianne
PATENT ASSIGNEE(S): Victor Chang Cardiac Research Institute, Australia
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

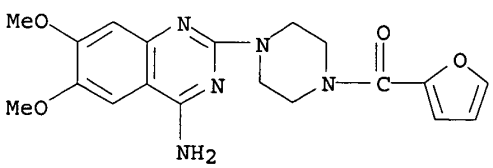
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602639	A1	19960201	WO 1995-AU437	19950719
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9529186	A1	19960216	AU 1995-29186	19950719

PRIORITY APPLN. INFO.: AU 1994-6934 19940719
WO 1995-AU437 19950719

AB The invention relates to modified adrenergic receptors being constitutively activating such that the receptor is activated through only one pathway. In particular, the invention relates to .alpha.1B-adrenergic receptors having an **amino acid** substitution at position 128 of the receptor such that the receptor is activated through the phospholipase C pathway. The invention also relates to cells expressing constitutively activating adrenergic receptors and methods using such cells.

IT **19216-56-9**, Prazosin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(mutant gene in transfected COS-1 cell produces constitutively activating adrenergic receptor with preference for phospholipase C pathway and use of cell for screening epinephrine and other compds.)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



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L8 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:997438 CAPLUS
DOCUMENT NUMBER: 124:76543
TITLE: Use of .alpha.1C-adrenergic receptor-specific compounds to treat benign prostatic hyperplasia
INVENTOR(S): Gluchowski, Charles; Forray, Carlos C.; Chiu, George; Branchek, Theresa A.; Wetzel, John M.; Hartig, Paul R.
PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528157	A1	19951026	WO 1995-US4203	19950404
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5578611	A	19961126	US 1994-228932	19940413
AU 9522404	A1	19951110	AU 1995-22404	19950404
AU 700304	B2	19981224		
EP 758894	A1	19970226	EP 1995-915559	19950404
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10502335	T2	19980303	JP 1995-526996	19950404

PRIORITY APPLN. INFO.:
US 1994-228932 A 19940413
US 1992-975867 A2 19921113
WO 1995-US4203 W 19950404

AB The subject invention provides a method of treating benign prostatic hyperplasia or inhibiting contraction of a prostate tissue in a subject in need thereof which comprises administering to the subject a therapeutically effective amt. of an .alpha.1C antagonist which binds to a human .alpha.1C adrenergic receptor with a binding affinity greater then 50-fold higher than the binding affinity with which the .alpha.1C antagonist binds to a human .alpha.1b adrenergic receptor, provided that the .alpha.1C antagonist is not 2,6-Dimethyl-4-(4-nitorphenyl)-1,4-dihydropyridine-3,5-dicarboxylic acid N-[3-(4.4-diphenylpiperidin-1-yl)-propyl] amide ester hydrochloride hydrate.

IT **19237-84-4P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(use of .alpha.1C-adrenergic receptor-specific compds. to treat benign prostatic hyperplasia)

RN 19237-84-4 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)-, monohydrochloride (9CI) (CA INDEX NAME)

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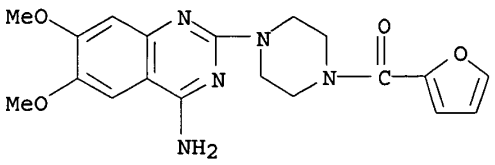

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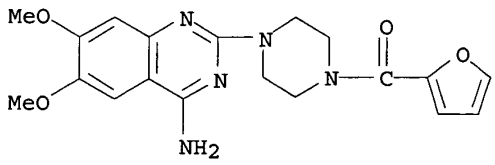
L8 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:554526 CAPLUS
DOCUMENT NUMBER: 123:189179
TITLE: Cloning, functional expression and tissue distribution of human .alpha.1C-adrenoceptor splice variants
AUTHOR(S): Hirasawa, Akira; Shibata, Katsushi; Horie, Kuniko; Takei, Yoshinori; Obika, Kenji; Tanaka, Teruo; Muramoto, Noriyuki; Takagaki, Kazuchika; Yano, Junichi; et al.
CORPORATE SOURCE: Department of Molecular, Cell Pharmacology, National Children's Medical Research Center, 3-35-31 Taishido, Setagaya-ku, Tokyo, 154, Japan
SOURCE: FEBS Letters (1995), 363(3), 256-60
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two isoforms of human .alpha.1C-adrenoceptor cDNA (.alpha.1C-2, .alpha.1C-3) were cloned and characterized. These isoforms are generated by alternative splicing and differ from the clone previously isolated (.alpha.1C-1) in their length and sequences of the C-terminal domain. Tissue distribution of mRNAs showed that these variants co-express with .alpha.1C-1 in the human heart, liver, cerebellum, and cerebrum. Despite the structural differences, functional expts. in transfected CHO cells showed that the 3 isoforms have similar ligand binding properties, and all couple with phospholipase C/Ca2+ signaling pathway.

IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cloning, functional expression and tissue distribution of human .alpha.1C-adrenoceptor splice variants)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:310940 CAPLUS
DOCUMENT NUMBER: 122:256516

[redacted]

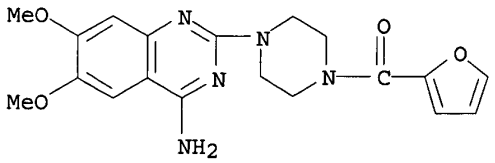
09/ 876,964

TITLE: Cloning and pharmacological characterization of human alpha-1 adrenergic receptors: sequence corrections and direct comparison with other species homologs
AUTHOR(S): Schwinn, Debra A.; Johnston, Geoffrey I.; Page, Stella O.; Mosley, Michael J.; Wilson, Katrina H.; Worman, Nicola P.; Campbell, Shannon; Fidock, Mark D.; Furness, L. Michael; et al.
CORPORATE SOURCE: Dep. Anesthesiol., Duke Univ. Med. Cent., Durham, NC, USA
SOURCE: J. Pharmacol. Exp. Ther. (1995), 272(1), 134-42
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cDNAs encoding 3 human .alpha.-1 adrenergic receptor (AR) subtypes were cloned and pharmacol. properties of the expressed receptor proteins were characterized. A no. of significant sequence corrections were identified and compared with previously published data, at both nucleotide and **amino acid** levels; the most major differences occur for the human .alpha.-1a/dAR. Pharmacol. characterization was performed simultaneously using 6 cloned .alpha.-1AR subtypes (human and rat .alpha.-1a/d, human and hamster .alpha.-1b, human and bovine .alpha.-1c) stably expressed in rat-1 fibroblasts at approx. equal receptor concns. (1-2 pmol/mg total protein). In general, human .alpha.-1AR subtypes have similar pharmacol. compared to their rat, hamster, and bovine homologs, although a few minor species differences important for .alpha.-1AR classification are noted. In addn., much lower inactivation (.apprx.20%) by the alkylating agent chloroethylclonidine is noted in this study compared to previous reports for both human and bovine .alpha.-1cAR membrane prepns. All 6 .alpha.-1AR subtypes couple to phosphoinositide hydrolysis in a pertussis toxin-insensitive manner, including the cloned human .alpha.-11/dAR which had not been expressed previously. In spite of significant sequence differences between human .alpha.-1ARs and their other species counterparts, previously established ligand selectivity remains fairly comparable. In summary, these data represent the first side-by-side comparison of pharmacol. properties between species homologs of .alpha.-1AR subtypes and should facilitate the development of .alpha.-1AR subtype selective drugs for clin. use.

IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(pharmacol. characterization of human .alpha.1-adrenergic receptors: sequence corrections and direct comparison with other species homologs)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)

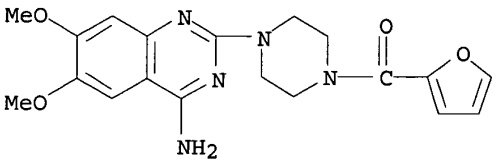


L8 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:280330 CAPLUS
DOCUMENT NUMBER: 122:46129
TITLE: Effect of chronic treatment with prazosin and L-arginine on the elevation of blood pressure during cold exposure
AUTHOR(S): Fregly, Melvin J.; Rossi, Fabian; Sun, Zhongjie;

Tumer, Nihal; Cade, J. Robert; Hegland, Donald; Yurekli, Muhittin
CORPORATE SOURCE: Departments of Physiol., Pharmacol. Med., Univ. Florida, Gainesville, FL, USA
SOURCE: Pharmacology (1994), 49(6), 351-62
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chronic exposure to cold (5.degree.C) is well known to increase both tyrosine hydroxylase (TH) activity in brown adipose tissue and systemic blood pressure. The effect of chronic dietary administration of the .alpha.-adrenergic antagonist, prazosin, and the **amino acid**, L-arginine, on both the elevation of blood pressure during exposure to cold and on TH activity and expression of TH mRNA in the adrenal glands of rats was studied. As obsd. previously, chronic exposure to cold increased systolic blood pressure significantly and induced cardiac hypertrophy. Chronic dietary treatment with prazosin (8 mg/kg food) and arginine (20 g/kg food) returned blood pressure to control levels, did not affect body wt. significantly, but failed to prevent cardiac hypertrophy. Both prazosin and L-arginine reduced the drinking response to administration of angiotensin II. Treatment with arginine and prazosin was accompanied by a significant increase in the urinary outputs of dopamine and L-DOPA. The 3 cold-treated groups (control, L-arginine and prazosin) had increases in plasma T3 and decreases in plasma T4 and plasma renin activity. Plasma concns. of epinephrine and norepinephrine were increased significantly in the L-arginine-treated group. TH mRNA and TH activity in the adrenal glands were increased in the 3 cold-treated groups and these measures were correlated directly and significantly with plasma norepinephrine and epinephrine concns. Although both prazosin and arginine prevented the cold-induced elevation of blood pressure, they did not prevent the increase in TH mRNA, TH activity or epinephrine in plasma. The protective effect of arginine and prazosin in cold-induced hypertension may be related both to their redn. in plasma renin activity and to a reduced responsiveness to angiotensin II, as well as to their abilities to increase the secretion of dopamine.

IT **19216-56-9**, Prazosin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prazosin and arginine prevention of chronic cold-induced hypertension)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:253820 CAPLUS
DOCUMENT NUMBER: 122:23985
TITLE: The heuristic-direct approach to theoretical quantitative structure-activity relationship analysis of .alpha.1-adrenoceptor ligands
AUTHOR(S): Fanelli, F.; Menziani, M. C.; Cocchi, M.; Leonardi, A.; De Benedetti, P. G.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, V. Campi 183, Modena, 41100, Italy

[redacted]

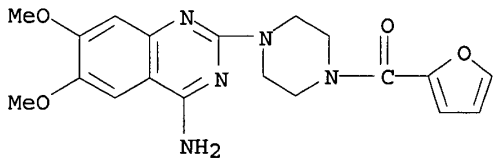
SOURCE: THEOCHEM (1994), 120(3), 265-76
CODEN: THEODJ; ISSN: 0166-1280
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The heuristic-direct quant. structure-activity relation approach was applied to 15 non-congeneric .alpha.1-adrenergic receptor (.alpha.1-AR) ligands interacting with the rat .alpha.1A/D-AR subtype. The good linear correlations, which have been obtained between calcd. binding energies and the pharmacol. affinities, allow one to predict the pharmacol. affinity of new ligands. Moreover, according to the .alpha.1A/D-receptor model proposed, it has been possible to speculate on the **amino acid** residues which are mainly involved in the interaction with the ligands. This novel procedure constitutes a powerful tool for the design of new selective leads based on explicit intermol. interactions and for suggesting site-directed mutagenesis studies, to give, interactively, further support and improvement to the predictive and interpretative aspects of the model.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(heuristic-direct approach to theor. QSAR anal. of .alpha.1-adrenoceptor ligands)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:247986 CAPLUS
DOCUMENT NUMBER: 122:24361

TITLE: Species orthologs of the alpha-2A adrenergic receptor: the pharmacological properties of the bovine and rat receptors differ from the human and porcine receptors

AUTHOR(S): O'Rourke, M. F.; Iversen, L. J.; Lomasney, J. W.; Bylund, D. B.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Nebraska Med. Cent., Omaha, NE, USA

SOURCE: J. Pharmacol. Exp. Ther. (1994), 271(2), 735-40
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

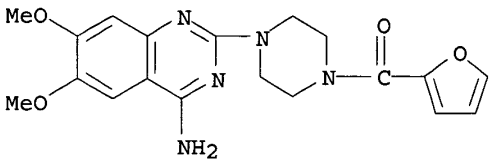
AB Four pharmacol. subtypes of the alpha-2 adrenergic receptor have been identified; however, only three subtypes exist in any given species. Although the alpha-2A adrenergic receptor, as defined by the human platelet, and the alpha-2D receptor, as defined in the bovine pineal, have very different pharmacol. characteristics, they are more similar to each other than either is to the alpha-2B or alpha-2C subtype. The human alpha-2-C10 clone (alpha-2A) and the rat RG20 clone have an 89% identity in their predicted **amino acid** sequence and are considered to be species orthologs. Although the expressed RG20 clone appears to have alpha-2D pharmacol., a careful comparison of its pharmacol. characteristics with the bovine pineal has not been reported previously. Based on the pKi values of a panel of 13 alpha-2 adrenergic agents that have been used previously to compare the alpha-2A, alpha-2B

and alpha-2C subtypes, the pharmacol. characteristics of the bovine pineal alpha-2D receptor appear to be very similar to the rat RG20 clone (correlation coeff., r, of 0.93). The porcine ortholog of the human alpha-2-C10 receptor has pharmacol. characteristics identical to the human alpha-2A receptor (r = 0.99). Because of its higher affinity for the alpha-2D receptor, [3H]RX 821002 is a better radioligand than [3H]rauwolscine for studying this receptor subtype.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pharmacol. of .alpha.2A-adrenergic receptor of bovine and rat differ from human and receptors)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:693353 CAPLUS

DOCUMENT NUMBER: 121:293353

TITLE: The rat homolog of the bovine .alpha.1c-adrenergic receptor shows the pharmacological properties of the classical .alpha.1A subtype

AUTHOR(S): Laz, Thomas M.; Forray, Carlos; Smith, Kelli E.; Bard, Jonathan A.; Vaysse, Pierre J.-J.; Branchek, Theresa A.; Weinshank, Richard L.

CORPORATE SOURCE: Synaptic Pharmaceutical Corp., Paramus, NJ, 07652, USA

SOURCE: Mol. Pharmacol. (1994), 46(3), 414-22
CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

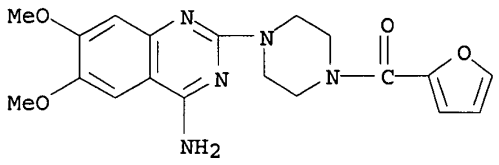
AB The cDNA for the rat .alpha.1c-adrenergic receptor (AR) was cloned using a probe derived from the bovine .alpha.1c-AR sequence. Clone rB7a has a 2.6-kb insert with a 1390-bp open reading frame and encodes a receptor of 466 amino acids. Cloned receptor has 91% **amino acid** identity with bovine .alpha.1c-AR. Rat .alpha.1c-AR mRNA was detected in tissues known to be enriched for the .alpha.1A-AR subtype, including vas deferens, heart, kidney, and hippocampus. It was absent from liver and spleen when assayed by Northern blot analyses and RNase protection assays. In COS-7 cells transfected with cDNAs encoding the 3 rat .alpha.1-ARs, WB-4101 and benoxathian had similar binding affinities for the .alpha.1a/d-AR and the .alpha.1c-AR and 10-fold lower affinities for the .alpha.1b-AR. The affinity of 5-methylurapidil was 10- and 30-fold higher at the .alpha.1c-AR than at the .alpha.1a/d- and .alpha.1b-ARs, resp. (S)-(+)-Niguldipine had high affinity for the rat .alpha.1c-AR, with 42- and 22-fold lower affinity at the .alpha.1a/d- and .alpha.1b-ARs, resp. Treatment of intact transfected COS-7 cells with chloroethylclonidine resulted in the inactivation of 19% of the .alpha.1c-ARs, in contrast to 72% and 85% inactivation of the .alpha.1a/d- and .alpha.1b-ARs, resp. Similarly to the other two .alpha.1-ARs, the rat .alpha.1c-AR is coupled to the activation of phospholipase C. The data suggest that rat .alpha.1c-AR cDNA encodes an .alpha.1-AR with pharmacol. properties previously defined for the .alpha.1A subtype found in tissues.

IT **19216-56-9**, Prazosin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(rat homolog of bovine .alpha.1c-adrenergic receptor shows pharmacol. properties of classical .alpha.1A subtype)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:500693 CAPLUS

DOCUMENT NUMBER: 121:100693

TITLE: The gene for human .alpha.1 adrenergic receptors and its cloning and expression

INVENTOR(S): Bard, Jonathan A.; Forray, Carlos; Weinshank, Richard L.

PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corp., USA

SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9408040	A1	19940414	WO 1993-US9187	19930924
W: AU, BR, CA, FI, HU, JP, KR, NO, NZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 663014	A1	19950719	EP 1993-922758	19930924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08505044	T2	19960604	JP 1993-509237	19930924
AU 677968	B2	19970515	AU 1993-51656	19930924
EP 1063291	A2	20001227	EP 2000-119362	19930924
EP 1063291	A3	20010425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1063292	A2	20001227	EP 2000-119363	19930924
EP 1063292	A3	20010425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5556753	A	19960917	US 1994-334698	19941104
US 5714381	A	19980203	US 1995-468939	19950606
US 5861309	A	19990119	US 1995-406855	19950821
AU 9734207	A1	19980129	AU 1997-34207	19970815
AU 718197	B2	20000406		

PRIORITY APPLN. INFO.:

US 1992-952789	A2	19920925
US 1992-952798	A	19920925
EP 1993-922758	A3	19930924
WO 1993-US9187	W	19930924
US 1994-334698	A1	19941104

AB Genes for human .alpha.1A, .alpha.1B, and .alpha.1C adrenergic receptors are cloned and expressed are cloned and expressed in animal cells for use in the development of pharmaceuticals and antibodies active against the receptor. Nucleic acid probes, and antisense oligonucleotides complementary to the .alpha.1 adrenergic receptor subtype genes are also described. The genes or cDNAs were cloned by screening human banks with sequences derived from the cognate rat receptor with genes reconstructed

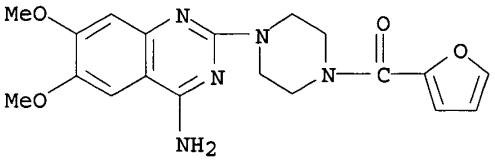
[redacted]

from overlapping clones as necessary. CDNAs were expressed in LM(tk-) cells using pCEXV-3 and the identity of the receptors confirmed by their pharmacologies. A series of potential antagonists (Terazosin, Indoramin, benzamidopiperidines, SKF-104856) were prepd. and tested for their efficacy.

IT **19216-56-9**, Prazosin
RL: BIOL (Biological study)
(as antagonist of of .alpha.1 adrenergic receptor subtypes, cloning and expression of receptor cDNAs in relation to)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:417836 CAPLUS

DOCUMENT NUMBER: 121:17836

TITLE: Kinetics of rearrangement and hydrolysis of **amino acid** derivatives of prazosin

AUTHOR(S): Pochopin, Nancy L.; Charman, William N.; Stella, Valentino J.

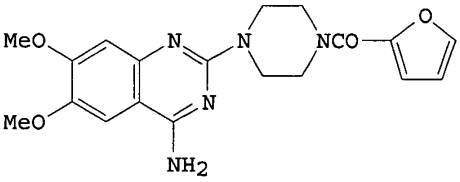
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. Kansas, Lawrence, KS, 66045, USA

SOURCE: Int. J. Pharm. (1994), 105(2), 169-76
CODEN: IJPHDE; ISSN: 0378-5173

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



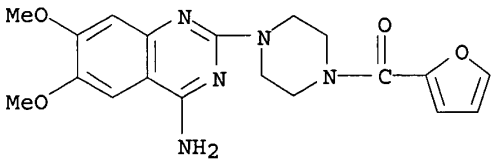
I

AB **Amino acid** amides of prazosin (I) have been synthesized as potential prodrugs to increase the water soly. of the parent compd. and target peptidase enzymes for cleavage of the prodrug in vivo (bioreversion). The .alpha.-**amino acid** derivs. degraded rapidly in aq. soln. at pH values >5 with half-lives on the order of 10-50 min. The rapid degrdn. of these derivs. was attributed to intramol. nucleophilic attack of the .alpha.-amine of the **amino acid** resulting in a rearranged product, not I. In the absence of a free .alpha.-amino group, greater stabilization was achieved and the primary route of degrdn. at all pH values was hydrolysis of the amide bond to give I.

IT **19216-56-9DP**, Prazosin, amino acyl derivs.

[redacted]

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis and rearrangement kinetics of, as prodrugs)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:147517 CAPLUS
DOCUMENT NUMBER: 116:147517
TITLE: Phencyclidine and phencyclidine metabolite assays, tracers, immunogens, antibodies and reagent kit
INVENTOR(S): Dubler, Robert Edward; Frintner, Mary Pat; Grote, Jonathan; Hawksworth, David James; Nam, Daniel S.; Wray, Larry Kay; Hadley, Gregg Allen; Hopkins, Hal Dayton; Ungemach, Frank S.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 459387	A2	19911204	EP 1991-108674	19910528
EP 459387	A3	19920902		
EP 459387	B1	19950920		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
US 5155212	A	19921013	US 1990-529988	19900529
AU 9177272	A1	19911205	AU 1991-77272	19910522
AU 643524	B2	19931118		
CA 2043372	AA	19911130	CA 1991-2043372	19910528
AT 128241	E	19951015	AT 1991-108674	19910528
ES 2080188	T3	19960201	ES 1991-108674	19910528
JP 04235199	A2	19920824	JP 1991-125955	19910529
US 5407834	A	19950418	US 1992-831762	19920427
PRIORITY APPLN. INFO.:			US 1990-529988	19900529
			US 1986-866193	19860521

OTHER SOURCE(S): MARPAT 116:147517
AB The present invention is directed to a fluorescence polarization assay for phenylcyclidine and phenylcyclidine derivs., to the various components needed for prepg. and carrying out such an assay, and to methods of making these components. Specifically, tracers, immunogens and (monoclonal) antibodies are disclosed, as well as methods for making them, and a reagent kit contg. them. The tracers and the immunogens are made from substituted phencyclidine compds. A fluorescein moiety is included in the tracer, while a poly(**amino acid**) forms a part of the immunogen. The assay is conducted by measuring the degree of polarization retention of plane polarized light that has been passed through a sample contg. antiserum and tracer. The assay has a high degree of specificity for phencyclidine and metabolites and analogs thereof, while minimizing mass reactivity to a host of other synthetic metabolites and naturally

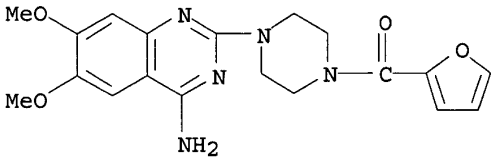
[redacted]

occurring compds.

IT **19216-56-9**, Prazosin
RL: ANST (Analytical study)
(phencyclidine fluorescence polarization immunoassay crossreactivity to)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:35353 CAPLUS

DOCUMENT NUMBER: 116:35353

TITLE: Isolation of rat genomic clones encoding subtypes of the .alpha.2-adrenergic receptor. Identification of a unique receptor subtype

AUTHOR(S): Lanier, Stephen M.; Downing, Sean; Duzic, Emir; Homcy, Charles J.

CORPORATE SOURCE: Cell. Mol. Res. Lab., Massachusetts Gen. Hosp., Boston, MA, 02114, USA

SOURCE: J. Biol. Chem. (1991), 266(16), 10470-8
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

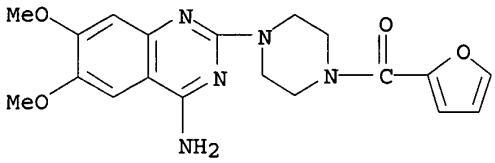
LANGUAGE: English

AB To isolate the rat genes encoding receptor subtypes a rat genomic library was screened with an oligonucleotide probe encompassing the third membrane span of the human C-4 .alpha.2-AR. Two intronless rat genes were isolated that encode distinct receptor subtypes (RG10, RG20). RG10 and RG20 encode proteins of 458 and 450 amino acids, resp., that are 56% homologous and possess the structural features expected of this class of membrane-bound receptors. RG10 identifies a mRNA species of .apprx.2500 nucleotides that is found primarily in brain, whereas RG20 identifies a larger mRNA species (.apprx.4000 nucleotides) that is found in several tissues including brain, kidney, and salivary gland. RG10 is 88% homologous to the human C-4 .alpha.2-AR and exhibits similar binding properties as detd. following transient expression of the receptor in COS-1 cells. RG20 exhibits ligand binding properties distinct from the 3 receptor subtypes identified by mol. cloning. Satn. binding studies indicate an affinity const. of 15 nM for the .alpha.2-AR antagonist [3H]rauwolscine, a value 6-20 times higher than that obsd. for the 3 cloned receptor subtypes. In competition binding studies the potency order of competing ligands for RG20 is phentolamine > idazoxan > yohimbine > rauwolscine > prazosin. Of the three previously cloned .alpha.2-AR, RG20 is most closely related to the human C-10 .alpha.2-AR (89% homol.) and is also capable of mediating adenylylcyclase inhibition as detd. following its stable expression in NIH-3T3 fibroblasts. However, in contrast to RG20, [3H] rauwolscine exhibits a KDof 2 nM for the C-109 receptor, and the potency order for competing ligands is rauwolscine .gtoreq. yohimbine > idazoxan > phentolamine > prazosin. RG20 and C-10 are also distinguished by their affinity for SKF-10478 (RG20 Ki = 531 nM, C-10 Ki = 101 nM), a compd. that may functionally distinguish pre- and postsynaptic .alpha.2-AR. These data suggest that RG20 represents a fourth .alpha.2-AR subtype distinct from the known .alpha.2A-C receptor subtypes.

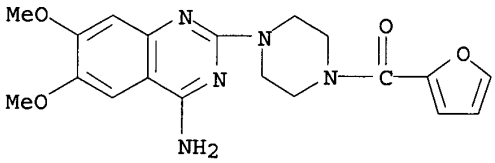
IT **19216-56-9**, Prazosin

[redacted]

RL: PRP (Properties)
(.alpha.2-adrenergic receptors RG10 and RG20 of rat binding affinity for)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:465752 CAPLUS
DOCUMENT NUMBER: 115:65752
TITLE: The rat .alpha.2-C4 adrenergic receptor gene encodes a novel pharmacological subtype
AUTHOR(S): Voigt, Mark M.; McCune, Susan K.; Kanterman, Robert Y.; Felder, Christian C.
CORPORATE SOURCE: Lab. Mol. Biol., NINDS, Bethesda, MD, 20817, USA
SOURCE: FEBS Lett. (1991), 278(1), 45-50
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rat gene and brain cDNA (pA2d) encoding the homolog of the human .alpha.-C4 adrenergic receptor subtype were isolated and characterized. RNA blots indicate that this gene is expressed in brain, heart, and kidney but not in lung, liver, or pancreas. Yohimbine, WB-4101, and prasozin all exhibited high affinity for this receptor in binding studies. Clonidine was more potent and efficacious than norepinephrine in inhibiting forskolin-stimulated cAMP prodn. in CHO cells expressing pA2d. Together, these data suggest that the .alpha.2-C4 gene product defines a previously undescribed pharmacol. subtype .alpha.2-adrenergic receptor.
IT **19216-56-9**, Prazosin
RL: PRP (Properties)
(.alpha.2-C4 adrenergic receptor of rat binding of)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:229391 CAPLUS
DOCUMENT NUMBER: 114:229391
TITLE: Preparation of tripeptides with N terminal carbamoyl or acyl groups as renin inhibitors
INVENTOR(S): Schoen, William R.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 50 pp.

[redacted]

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

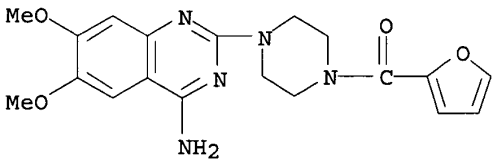
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 347987	A2	19891227	EP 1989-201563	19890615
EP 347987	A3	19910102		
R: CH, DE, FR, GB, IT, LI, NL				
JP 02040398	A2	19900209	JP 1989-155939	19890620

PRIORITY APPLN. INFO.: US 1988-209749 19880620
OTHER SOURCE(S): MARPAT 114:229391

AB Q-A-B-E-G-J [I; Q = amino, HO, alkoxy, etc.; A = CO, OC(O); B, E = .alpha.-**amino acid** residue; G = substituted iminotrimethylenecarbonyl; J = substituted amino, substituted alkoxy, etc.], useful as renin inhibitors (no data) were prepd. H2NCMe2CONHCH2CH2CO-Phe-His-NHCHQCH(OH)CH2CO-NHCHMePr (Q = cyclohexylmethyl) was prepd. in many steps starting from HO2CCMe2CH2CO2Me and PhCH2OH. I are useful in treatment of hypertension and congestive heart failure and may be formulated with many known diuretics, .alpha.- and .beta.-adrenergic blocking agents, Ca channel blockers, vasodilators, and central nervous system agents.

IT **19216-56-9**, Prazosin
RL: RCT (Reactant)
(antihypertensive pharmaceuticals contg. renin inhibitors and)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:30005 CAPLUS
DOCUMENT NUMBER: 114:30005
TITLE: Poly(.alpha.-**amino acid**)-drug conjugates - a biodegradable injectable drug delivery system
AUTHOR(S): Li, Xiaoling; Bennett, David B.; Adams, Nathan W.; Kim, Sung Wan
CORPORATE SOURCE: Cent. controlled Chem. Delivery, Univ. Utah, Salt Lake City, UT, 84108, USA
SOURCE: Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.) (1990), 31(2), 198-9
CODEN: ACPPAY; ISSN: 0032-3934
DOCUMENT TYPE: Journal
LANGUAGE: English

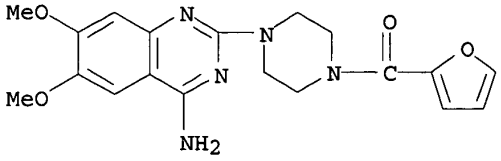
AB A prazosin (I) conjugate with poly(3-hydroxypropyl-L-glutamine) (PHPG) and naltrexone (II) conjugates with hydroxypropyl-L-glutamine-leucine copolymer [p(HPG/LEU)] were prepd. for controlled release injections. I-PHPG conjugate with a particle size 17-28 .mu.m gave a const. release for 3 wk. Drug release from II-p(HPG/LEU) conjugates increased with decreasing particle size. In in vivo studies, following the initial burst, nearly const. drug plasma levels were achieved for 2 wk for I-PHPG

conjugates and 30 days for the II-p(HPG/LEU) conjugates.

IT **19216-56-9DP**, Prazosin, reaction products with poly(hydroxypropylglutamine)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and controlled drug release from injections contg.)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:625427 CAPLUS

DOCUMENT NUMBER: 113:225427

TITLE: Expansion of the .alpha.2-adrenergic receptor family: cloning and characterization of a human .alpha.2-adrenergic receptor subtype, the gene for which is located on chromosome 2

AUTHOR(S): Lomasney, Jon W.; Lorenz, Wulfing; Allen, Lee F.; King, Klim; Regan, John W.; Yang-Feng, Theresa L.; Caron, Marc G.; Lefkowitz, Robert J.

CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(13), 5094-8
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

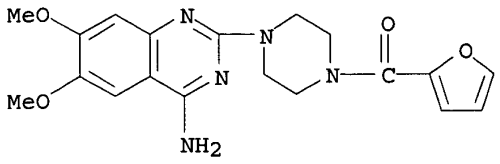
AB Pharmacol., biochem., and genetic analyses have demonstrated the existence of multiple .alpha.2-adrenergic receptor (.alpha.2AR) subtypes. A human .alpha.2AR gene was cloned by using the polymerase chain reaction with oligonucleotide primers homologous to conserved regions of the previously cloned .alpha.2ARs, the genes for which are located on human chromosomes 4 (C4) and 10 (C10). The deduced **amino acid** sequence encodes a protein of 450 amino acids whose putative topol. is similar to that of the family of guanine nucleotide-binding protein-coupled receptors, but whose structure most closely resembles that of the .alpha.2ARs. Competition curve anal. of the binding properties of the receptor expressed in COS-7 cells with a variety of adrenergic ligands demonstrates a unique .alpha.2AR pharmacol. Hybridization with somatic cell hybrids shows that the gene for this receptor is located on chromosome 2. Northern blot anal. of various rat tissues shows expression in liver and kidney. The unique pharmacol. and tissue localization of this receptor suggest that this is an .alpha.2AR subtype not previously identified by classical pharmacol. or ligand binding approaches.

IT **19216-56-9**, Prazosin
RL: PRP (Properties)
(binding affinity of, for .alpha.2-adrenergic receptor subtypes of human)

RN 19216-56-9 CAPLUS

CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)

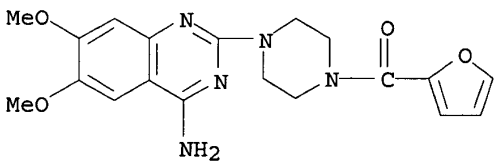
[redacted]



L8 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:493461 CAPLUS
DOCUMENT NUMBER: 113:93461
TITLE: Molecular cloning and expression of the cDNA for a novel .alpha.1-adrenergic receptor subtype
AUTHOR(S): Schwinn, Debra A.; Lomasney, Jon W.; Lorenz, Wulfing; Szklut, Pamela J.; Fremeau, Robert T., Jr.; Yang-Feng, Teresa L.; Caron, Marc G.; Lefkowitz, Robert J.; Cotecchia, Susanna
CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA
SOURCE: J. Biol. Chem. (1990), 265(14), 8183-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel .alpha.1-adrenergic receptor subtype has been cloned from a bovine brain cDNA library. The deduced **amino acid** sequence is that of a 466-residue polypeptide. The structure is similar to that of the other adrenergic receptors as well as the larger family of G protein-coupled receptors that have a presumed 7-membrane-spanning domain topog. The greatest sequence identity of this receptor protein is with the previously cloned hamster .alpha.1B-adrenergic receptor being .apprx.72% within the presumed membrane-spanning domains. Localization on different human chromosomes provides evidence that the bovine cDNA is distinct from the hamster .alpha.1B-adrenergic receptor. The bovine cDNA clone expressed in COS7 cells revealed 10-fold higher affinity for the .alpha.1-adrenergic antagonists WB4101 and phentolamine and the agonist oxymetazoline as compared with the .alpha.1B receptor, results similar to pharmacol. binding properties described for the .alpha.1A receptor. Despite these similarities in pharmacol. profiles, the bovine .alpha.1-adrenergic receptor is sensitive to inhibition by the alkylating agent chloroethylclonidine unlike the .alpha.1A-adrenergic receptor subtype. In addn., a lack of expression in tissues where the .alpha.1A subtype exists suggests that this receptor may actually represent a novel .alpha.1-adrenergic receptor subtype not previously appreciated by pharmacol. criteria.

IT **19216-56-9**, Prazosin
RL: BIOL (Biological study)
(.alpha.1-adrenergic receptor of ox brain binding of, hamster receptor in relation to)
RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:173277 CAPLUS
DOCUMENT NUMBER: 112:173277
TITLE: Cloning, sequence analysis, and permanent expression of a human .alpha.2-adrenergic receptor in Chinese hamster ovary cells. Evidence for independent pathways of receptor coupling to adenylate cyclase attenuation and activation
AUTHOR(S): Fraser, Claire M.; Arakawa, Shoji; McCombie, W. Richard; Venter, J. Craig
CORPORATE SOURCE: Natl. Inst. Neurol. Disord. Stroke, NIH, Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1989), 264(20), 11754-61
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

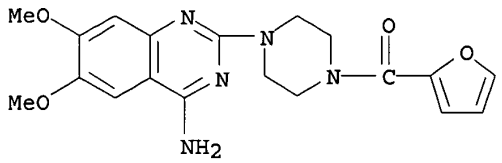
AB The gene encoding a human .alpha.2-adrenergic receptor was isolated from a human genomic DNA library using a 367-base-pair fragment of Drosophila genomic DNA that exhibited 54% identity with the human .beta.2-adrenergic receptor and 57% identity with the human .alpha.2-adrenergic receptor. The nucleotide sequence of a fragment contg. the human .alpha.2-receptor gene and 2.076 kilobases of untranslated 5' sequence was detd., and potential upstream regulatory regions were identified. This gene encodes a protein of 450 amino acids and was identified as an .alpha.2-adrenergic receptor by homol. with published sequences and by pharmacol. characterization of the protein expressed in cultured cells. Permanent expression of the .alpha.2-receptor was achieved by transfecting CHO cells which lack adrenergic receptors with a 1.5-kilobase NcoI-HindIII fragment of the genomic clone contg. the coding region of the gene. The .alpha.2-receptor expressed in CHO cells displayed pharmacol. characteristic of an .alpha.2A-receptor subtype with a high affinity for yohimbine (Ki = 1 nM) and a low affinity for prazosin (Ki = 10,000 nM). Agonists displayed a rank order of potency in radioligand binding assays of para-aminoclonidine .gtoreq. UK-14304 > (-)-epinephrine > (-)-norepinephrine > (-)-isoproterenol, consistent with the identification of this protein as an .alpha.2-receptor. The role of the .alpha.2-receptor in modulating intracellular cAMP concns. was investigated in 3 transfected cell lines expressing 50, 200, and 1200 fmol of receptor/mg membrane protein. At low concns. (1-100 nM), (-)-epinephrine attenuated forskolin-stimulated cAMP accumulation by .ltoreq.60% in a receptor d.-dependent manner. At epinephrine concns. >100 nM, cAMP levels were increased .ltoreq.140% of the forskolin-stimulated level. Pertussis toxin pretreatment of cells eliminated .alpha.2-receptor-mediated attenuation of forskolin-stimulated cAMP levels and enhanced the receptor d.-dependent potentiation of forskolin-stimulated cAMP concns. from 3 to 8-fold. Potentiation of forskolin-stimulated cAMP levels was also elicited by the .alpha.2-adrenergic agonists, UK-14304 and para-aminoclonidine, and blocked by the .alpha.2-adrenergic antagonist yohimbine, but not by the .alpha.1-adrenergic antagonist prazosin or the .beta.-adrenergic antagonist propranolol. .alpha.2-Receptor-mediated potentiation of forskolin-stimulated adenylate cyclase activity is apparently not due to activation of phospholipase C, as epinephrine had no effect on phosphoinositide hydrolysis in transfected cells, or to Na+/H+ exchange, as the potential was unaffected by ethylisopropylamiloride at concns. .ltoreq.100 .mu.M. The nonselective phospholipase A2 inhibitor quinacrine antagonized the .alpha.2-receptor-mediated stimulation of cAMP prodn. in pertussis toxin-treated cells in a dose-dependent manner. In cells treated with quinacrine in the absence of pertussis toxin, epinephrine produced .ltoreq.90% inhibition of forskolin-stimulated cAMP concns. in a dose-dependent manner with no increases in cAMP prodn. Apparently, the human .alpha.2-adrenergic receptor in CHO cells may simultaneously couple to .gtoreq.1 effector, including a pertussis toxin-sensitive attenuation

of adenylate cyclase and a pertussis toxin-insensitive pathway that results in potentiation of intracellular cAMP levels.

IT **19216-56-9**, Prazosin
RL: PRP (Properties)
(forskolin-stimulated cAMP formation response to, in CHO cells contg. cloned human .alpha.2-adrenergic receptor gene)

RN 19216-56-9 CAPLUS

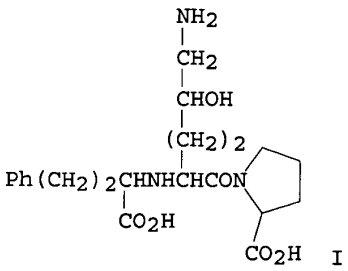
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:209445 CAPLUS
DOCUMENT NUMBER: 102:209445
TITLE: N-Carboxymethyl-substituted lysyl and .alpha.-(.epsilon.-aminoalkyl)glycyl **amino acid** antihypertensive agents
INVENTOR(S): Patchett, Arthur A.; Wu, Mu T.
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: S. African, 51 pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8302508	A	19841128	ZA 1983-2508	19830411
PRIORITY APPLN. INFO.:			US 1982-367531	19820412

GI



I

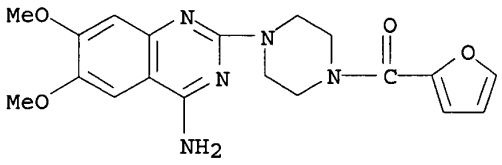
AB Novel N-carboxymethyl substituted lysyl and .alpha.-(.epsilon.-aminoalkyl)glycyl amino acids, which are inhibitors of angiotensin I-converting enzymes, were formulated in pharmaceutical compns. and used to treat hypertension. I was treated with 4-phenyl-2-oxobutanoic acid [710-11-2] to give N-[6-benzyloxycarbonylamino-2-(1-carboxy-3-phenylpropylamino)-5-hydroxyhexanoyl]-L-proline [96359-86-3], and the latter compd. was hydrogenated to give N-[6-amino-2-(1-carboxy-3-phenylpropylamino)-5-hydroxyhexanoyl-L-proline (II) [96359-87-4] which

[redacted]

has antihypertensive activity. The synthesis of these amino acids was described. E.g., 5-hydroxy-L-lysine [1190-94-9] was converted to N-(2-amino-6-benzyloxycarbonylamino-5-hydroxyhexanoyl)-L-proline (I) [96359-85-2] by a series of blocking and deblocking reactions and reaction with L-proline tert-Bu ester [2812-46-6]. Compns. contg. the title compds. and known antihypertensives were described.

IT **19216-56-9**
RL: BIOL (Biological study)
(antihypertensive compn. contg. **amino acid** derivs. and)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)

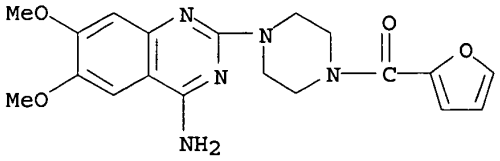


L8 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:179260 CAPLUS
DOCUMENT NUMBER: 102:179260
TITLE: Interaction of tachykinins with an adrenergic receptor in the rat urinary bladder
AUTHOR(S): Mathison, Ronald; Solomos, Danielle
CORPORATE SOURCE: Dep. Anim. Biol., Univ. Geneva, Geneva, 1205, Switz.
SOURCE: Eur. J. Pharmacol. (1985), 109(3), 327-33
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

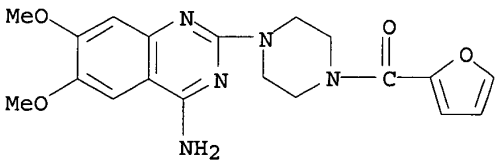
AB The rat urinary bladder was examd. as a model for studying tachykinin receptors. The order of potency, the maximal effect, and the slope of the dose-response curve were examd. with 6 tachykinins, substance P (SP) [33507-63-0], physalemin [2507-24-6], phyllomedusin [26145-48-2], uperolein [55601-63-3], eledoisin [69-25-0], kassinin [63968-82-1] and several substance P fragments, 2-11-SP [53749-61-4], 3-11-SP [51165-11-8], 4-11-SP [53749-60-3], and 6-11-SP [51165-07-2]. The tachykinin receptor on the rat urinary bladder preferentially bound tachykinins having a hydrophilic **amino acid** residue in position 5-6, as occurs with physalemin, phyllomedusin, eledoisin, and kassinin. The N-terminal of the tachykinins and in particular substance P is suggested to play a major role in regulating affinity, intrinsic activity, and the slope of the dose-response curve. An accessory binding site assocd. with the tachykinin receptor on rat urinary bladder was also identified. This accessory site binds the N-terminal amino acids of the tachykinins as well as some .alpha.-adrenergic compds. (phentolamine [50-60-2], prazosin [**19216-56-9**], noradrenaline [51-41-2], or adrenaline [51-43-4] in the presence of propranolol). When the accessory binding site is occupied by adrenergic compds., the affinity of the tachykinins is markedly reduced. Apparently catecholamines may have a modulatory influence on tachykinin activity on the rat urinary bladder.

IT **19216-56-9**
RL: BIOL (Biological study)
(bladder contraction response to tachykinins and, receptor in relation to)

RN 19216-56-9 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



L8 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:200113 CAPLUS
DOCUMENT NUMBER: 96:200113
TITLE: Tritium nuclear magnetic resonance spectroscopy. Part 13. Tritium labeled neurochemicals
AUTHOR(S): Bloxsidge, James P.; Elvidge, John A.; Gower, Marion; Jones, John R.; Evans, E. Anthony; Kitcher, J. Philip; Warrell, David C.
CORPORATE SOURCE: Dep. Chem., Univ. Surrey, Guildford, GU2 5XH, UK
SOURCE: J. Labelled Compd. Radiopharm. (1981), 18(8), 1141-65
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fifty neurochem. amino acids, catecholamines, and alkaloids were labeled with 3H by 8 methods, and the extent of labeling was detd. by 3H NMR.
IT **80573-46-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tritium NMR of)
RN 80573-46-2 CAPLUS
CN Piperazine, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl)-, labeled with tritium, monohydrochloride (9CI) (CA INDEX NAME)



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FILE 'REGISTRY' ENTERED AT 16:43:58 ON 30 AUG 2002
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L2 50 S L1
L3 2396 S L1 FUL
L4 2396 S L3 NOT (BENZO WITH TRIAZIN?)

FILE 'CAPLUS' ENTERED AT 16:46:00 ON 30 AUG 2002
L5 3101 S L4
L6 0 S L5 AND (AMINO ADJ ACID)
L7 427027 S (AMINO ACID)

09/ 876,964

L8 39 S L5 AND L7

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	182.08	335.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-24.16	-24.16

STN INTERNATIONAL LOGOFF AT 16:50:00 ON 30 AUG 2002